Central pain location in SCN9A-associated SFN: an fMRI pilot study.

Published: 02-11-2015
Last updated: 19-04-2024

To explore whether patients with SCN9A-associated SFN have an abnormal brain activation pattern on resting state fMRI and altered structural connectivity on DTI versus age- and gender-matched healthy controls. With this knowledge, objective pain...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peripheral neuropathies
Study type	Observational non invasive

Summary

ID

NL-OMON47720

Source
ToetsingOnline

Brief title
fMRI in small fiber neuropathy

Condition

- Peripheral neuropathies

Synonym
small fiber neuropathyhttps://www.toetsingonline.nl/to/ccmo_monitor.nsf/allabrs/53441-06?EditDocument#

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: central pain, functional MRI, SCN9A-mutation, small fiber neuropathy

Outcome measures

Primary outcome

Concerning the fMRI, change of connectivity in the central executive network (CEN) and sensorimotor network (SMN) is the primary endpoint.

Change in brain connectivity have been observed in several neuropathic pain conditions affecting mainly the networks mentioned above: SMN tend to show hyperconnectivity while CEN hipoconnectivity. Concerning DTI, the study parameters are fractional anisotropy (FA) and axial diffusivity (AD).

Secondary outcome

Not applicable

Study description

Background summary

Small fiber neuropathy (SFN) is a form of peripheral neuropathy, which is characterized by neuropathic pain and autonomic dysfunction. Mutations in SCN9A, the gene encoding for the voltage-gated sodium channel NaV1.7, are associated with SFN. SCN9A-associated SFN often results in chronic neuropathic pain, which is difficult to treat. Chronic neuropathic pain may cause structural and functional changes in the brain. Until now, only one small study examined the structural and functional changes of the brain in SFN patients. No studies have been performed in strictly defined SFN patients. Therefore it would be interesting to explore whether in SFN patients with an SCN9A mutation, the genotype will lead to a distinct brain activation pattern on functional MRI (fMRI) and if the integrity or structural connectivity of the brain is altered using diffusion tensor imaging (DTI). This may provide a better understanding of the pathophysiological pathways for chronic pain and might serve as a biomarker for evaluating therapy.
We hypothesize that SCN9A-associated SFN will lead to a specific brain

activation pattern on fMRI and altered structural connectivity on DTI.

Study objective

To explore whether patients with SCN9A-associated SFN have an abnormal brain activation pattern on resting state fMRI and altered structural connectivity on DTI versus age- and gender-matched healthy controls. With this knowledge, objective pain measurement for patients with SFN may serve as a biomarker in evaluating efficacy of targeted therapy.

Study design

This is a case-control study. It is a type of observational study in which three existing groups differing in outcome are identified and compared. Case-control studies are often used to identify factors that may contribute to a medical condition by comparing subjects who have that condition/disease with patients who do not have the condition/disease.
Three subjects from each group receive an additional MRI-scan (Tesla 7.0).

Study burden and risks

This pilot study provides a low burden for the participant. The participant will visit our hospital only once. This visit lasts up to 90 minutes and will consist of a anatomical MRI-scan, fMRI-scan and DTI-scan (max. 60 minutes) and completing four questionnaires (remaining time). The contact time is estimated for 120 minutes, including the intake and signing the informed consent forms. Halfway the fMRI scan, a so-called advanced thermal stimulation (ATS) will be performed with heat and cold stimulation. This can be unpleasant but is usually not experienced as painful.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patient group (SCN9A-associated SFN) (n <= 20)
a. Male and/or female subjects between the ages of 18 and 80 years.
b. Presence of a clinical diagnosis of small fiber neuropathy, according to international criteria and presence of confirmed abnormality on intra-epidermal nerve fiber density evaluation and/or Quantitative Sensory Testing.
c. A mutation in the SCN9A gene, confirmed by sequencing, with possible, probable or certain pathogenicity according to international criteria.
d. Presence of pain due to SFN for at least 3 months and an average self-reported pain score of at least 5.
e. Subjects must give informed consent by signing and dating an informed consent form., Patient group (SFN without a gene mutation)
a. Male and/or female subjects between the ages of 18 and 80 years.
b. Presence of a clinical diagnosis of SFN, according to international criteria,1, 52, 53 including a decreased intra-epidermal nerve fiber density IENFD in skin biopsy.
c. No mutation in the SCN9A, SCN10A or SCN11A gene, confirmed by sequencing.
d. Presence of pain due to SFN for at least 3 months and an average self-reported pain score of at least 5.
e. Subjects must give informed consent by signing and dating an informed consent form., Control group (n <= 20)
a. Male and/or female subjects between the ages of 18 and 80 years.
b. Subjects must give informed consent by signing and dating an informed consent form.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded

from participation in this study:
a. Major depression according to DSM-V criteria or a history of major psychiatric disease.
b. (History with) alcohol abuse
c. Hospital Anxiety and Depression Scale (HADS) * 14
d. Subjects who have another pain syndrome than small fiber neuropathy.
e. Contraindications for undergoing MRI: pacemaker, metallic foreign body (including aneurysm clip in the brain), claustrophobia, pregnancy, neurostimulator, pacemaker or other kinds of implanted devices or insulin pump. In case of cardiac valve replacement of ossicular replacement prosthesis the radiologist will be consulted.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-05-2018
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	02-11-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	19-09-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-06-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-08-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL53441.068.15